

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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In re application of:

Hartley *et al.*

Appl. No. 09/517,466

Filed: March 2, 2000

For: **Compositions and Methods for  
Use in Recombinational Cloning  
of Nucleic Acids**

Art Unit: 1655

Examiner: Johannsen, D.

Atty. Docket: 0942.4680003/RWE/BJD

**Letter**

Commissioner for Patents  
Washington, D.C. 20231

*Via Hand Carry to Art Unit 1655  
Attn: Examiner D. Johannsen*


Sir:

Applicants submit the following documents for appropriate action by the U.S.  
Patent and Trademark Office:

1. Information Disclosure Statement (in duplicate);
2. 67 pages of Form PTO-1449 citing 254 documents;
3. A copy of each of the 254 cited documents; and
4. One return postcard.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Brian J. Del Buono  
Attorney for Applicants  
Registration No. 42,473

Date: Jan. 26, 2001

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**Information Disclosure Statement**

Commissioner for Patents  
Washington, D.C. 20231

Sir:

Listed on accompanying Form PTO-1449 are documents that may be considered material to the examination of this application, in compliance with the duty of disclosure requirements of 37 C.F.R. §§ 1.56, 1.97 and 1.98. A copy of each document is submitted herewith.

Where the publication date of a listed document does not provide a month of publication, the year of publication of the listed document is sufficiently earlier than the effective U.S. filing date and any foreign priority date so that the month of publication is not in issue. Applicants have listed publication dates on the attached PTO-1449 based on information presently available to the undersigned. However, the listed publication dates should not be construed as an admission that the information was actually published on the date indicated.

The Examiner's attention is directed to co-pending U.S. Patent Application Nos.

09/177,387, filed October 23, 1998,

09/233,492, filed January 20, 1999,

09/296,280, filed April 22, 1999,  
09/296,281, filed April 22, 1999,  
09/432,085, filed November 2, 1999,  
09/438,358, filed November 12, 1999,  
09/498,074, filed February 4, 2000,  
09/517,466, filed March 2, 2000,  
09/518,188, filed March 2, 2000,  
09/648,790, filed August 28, 2000,  
09/695,065, filed October 25, 2000, and  
(TBA), filed December 11, 2000;

which are directed to related technical subject matter. The identification of these U.S. Patent Applications is not to be construed as a waiver of secrecy as to that application now or upon issuance of the present application as a patent. The Examiner is respectfully requested to consider the cited applications and the art cited therein during examination.

Applicants reserve the right to establish the patentability of the claimed invention over any of the information provided herewith, and/or to prove that this information may not be prior art, and/or to prove that this information may not be enabling for the teachings purportedly offered.

This statement should not be construed as a representation that a search has been made, or that information more material to the examination of the present patent application does not exist. The Examiner is specifically requested not to rely solely on the material submitted herewith. It is further understood that the Examiner will consider information that had been cited or submitted to the U.S. Patent and Trademark Office in a prior application relied on under 35 U.S.C. § 120. 1138 OG 37, 38 (May 19, 1992).

This Information Disclosure Statement is being filed before the mailing date of a first Office Action on the merits. No statement or fee is required.

It is respectfully requested that the Examiner initial and return a copy of the enclosed PTO-1449, and to indicate in the official file wrapper of this patent application that the documents have been considered.

The U.S. Patent and Trademark Office is hereby authorized to charge any fee deficiency, or credit any overpayment, to our Deposit Account No. 19-0036. A duplicate copy of this pleading is enclosed.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.



Brian J. Del Buono  
Attorney for Applicants  
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FORM PTO-1449  <u>INFORMATION DISCLOSURE STATEMENT</u>	ATTY. DOCKET NO. 0942.4680003	APPLICATION NO. 09/517,466
	APPLICANT Hartley et al.	
	FILING DATE March 2, 2000	GROUP 1655

U.S. PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA1	4,673,640	06/16/1987	Backman, K.C.	435	68	04/30/1984
	AB1	4,743,546	05/10/1998	Backman et al.	435	108	02/13/1985
	AC1	4,959,317	09/25/1990	Sauer B.L.	435	172.3	04/29/1987
	AD1	5,227,288	07/13/1993	Blattner, F.R.	435	6	10/01/1990
	AE1	5,354,668	10/11/1994	Auerbach, J.I.	435	91.1	10/15/1993
	AF1	5,434,066	07/18/1995	Bebbee, R.L., et al.	435	172.3	03/15/1994
	AG1	5,470,727	11/28/1995	Mascarenhas et al.	435	172.3	12/21/1993
	AH1	5,591,609	01/07/1997	Auerbach, J.I.	435	91.2	02/03/1995
	AI1	5,614,389	03/25/1997	Auerbach, J.I.	435	91.2	09/26/1995
	AJ1	5,635,381	06/03/1997	Hooykaas et al.	435	172.3	01/20/1995
	AK1	5,658,772	08/19/1997	Odell et al.	435	172.3	07/27/1994

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL1	EP 0 160 571 A2	11/06/1985	Europe			Yes No
	AM1	EP 0 300 422	01/25/1989	Europe			Yes No
	AN1	WO 91/02801	03/07/1991	WIPO			Yes No
	AO1	WO 91/16427	10/31/1991	WIPO			Yes No
	AP1	WO 92/20791	11/26/1992	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
AR	<u>1</u>	Abremski, K., and Gottesman, S., "Purification of the Bacteriophage $\lambda$ xis Gene Product Required for $\lambda$ Excisive Recombination," <i>J. Biol. Chem.</i> 257(16):9658-9662, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1982).	
AS	<u>1</u>	Abremski, K., and Hoess, R., "Bacteriophage P1 Site-specific Recombination - Purification and Properties of the Cre Recombinase Protein," <i>J. Biol. Chem.</i> 259:1509-1514, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1984).	
AT	<u>1</u>	Abremski, K., et al., "Bacteriophage P1 Cre-loxP Site-specific Recombination: Site-specific DNA Topoisomerase Activity of the Cre Recombination Protein," <i>J. Biol. Chem.</i> 261(1):391-396, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1986).	

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<b>EXAMINER:</b> Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.	

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB-CLASS	FILING DATE
	AA2	5,677,170	10/14/1997	Devine et al.	435	20.1	03/02/1994
	AB2	5,677,177	10/14/1997	Wahl et al.	435	325	06/07/1995
	AC2	5,710,248	01/20/1998	Grose, C.F.	530	327	07/29/1996
	AD2	5,723,765	03/03/1998	Oliver et al.	800	208	06/07/1995
	AE2	5,733,733	03/31/1998	Auerbach, J.I.	435	6	02/01/1996
	AF2	5,733,743	03/31/1998	Johnson et al.	435	320.1	06/10/1996
	AG2	5,744,336	04/28/1998	Hodges et al.	435	172.3	03/08/1996
	AH2	5,766,891	06/16/1998	Shuman, S.	435	91.41	12/19/1994
	AI2	5,776,449	07/07/1998	Baum et al.	424	93.2	09/20/1996
	AJ2	5,830,707	11/03/1998	Bushman, F.D.	435	69.7	06/05/1995
	AK2	5,837,242	11/17/1998	Holliger et al.	424	136.1	05/14/1996

FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL2	WO 93/15191	08/05/1993	WIPO			Yes No
	AM2	WO 93/19172	09/30/1993	WIPO			Yes No
	AN2	CA 2,141,412	02/17/1994	Canada			Yes No
	AO2	WO 94/17176	08/04/1994	WIPO			Yes No
	AP2	WO 95/00555	01/05/1995	WIPO			Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	2	Abremski, K., et al., "Studies on the Properties of P1 Site-Specific Recombination: Evidence for Topologically Unlinked Products Following Recombination," Cell 32:1301-1311, Cell Press, Cambridge, MA (1993).
	AS	2	Adams, D.E., et al., "Cre-lox Recombination in <i>Escherichia coli</i> Cells: Mechanistic Differences from the <i>in Vitro</i> Reaction," J. Mol. Biol. 226:661-673, Academic Press, Inc., New York, NY (1992).
	AT	2	Andrews, B.J., et al., "The FLP Recombinase of the 2 $\mu$ Circle DNA of Yeast: Interaction with Its Target Sequences," Cell 40:795-803, Cell Press, Cambridge, MA (1985).

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
	AA3	5,843,772	12/01/1998	Devine, S.E., et al.	435	69.1	11/18/1994
	AB3	5,851,808	12/22/1998	Elledge et al.	435	172.3	02/28/1997
	AC3	5,858,657	01/12/1999	Winter et al.	435	6	06/07/1995
	AD3	5,871,907	02/16/1999	Winter et al.	435	6	03/31/1994
	AE3	5,874,259	02/23/1999	Szybalski, W.	435	91.1	11/21/1997
	AF3	5,888,732	03/30/1999	Hartley et al.	435	6	06/07/1996
	AG3	5,916,804	06/29/1999	Bushman, F.D.	435	325	04/17/1998
	AH3	5,919,676	07/06/1999	Graham et al.	435	172.3	06/07/1995
	AI3	5,928,914	07/27/1999	Leboulch et al.	435	172.3	11/05/1996
	AJ3	5,989,872	11/22/1999	Luo et al.	435	91.2	08/12/1997
	AK3	6,010,884	01/04/2000	Griffiths et al.	435	69.7	05/29/1996

## FOREIGN PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB- CLASS	TRANSLATION
	AL3	WO 97/06265	02/20/1997	WIPO			Yes No
	AM3	WO 97/09436	03/13/1997	WIPO			Yes No
	AN3	WO 97/25446	07/17/1997	WIPO			Yes No
	AO3	WO 97/32481	09/12/1997	WIPO			Yes No
	AP3	WO 98/10086	03/12/1998	WIPO			Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

AR	<u>3</u>	Andrews, B.J., et al., "Interaction of the FLP Recombinase of the <i>Saccharomyces cerevisiae</i> 2 $\mu$ m Plasmid with Mutated Target Sequences," <i>Mol. Cell. Biol.</i> 6:2482-2489, American Society for Microbiology, Washington, D.C. (1986).
AS	<u>3</u>	Anton, M., and Graham, F.L., "Site-Specific Recombination Mediated by an Adenovirus Vector Expressing the Cre Recombinase Protein: a Molecular Switch for Control of Gene Expression," <i>J. Virol.</i> 69:4600-4606, American Society for Microbiology, Washington, D.C. (1995).
AT	<u>3</u>	Araki, H., et al., "Site-specific Recombinase, R, Encoded by Yeast Plasmid pSR1," <i>J. Mol. Biol.</i> 225:25-37, Academic Press, Inc., New York, NY (1992).

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	AA4	6,040,430	03/21/2000	Stewart	530	358	12/26/1995
	AB4	6,063,627	06/16/2000	McVey et al.	435	440	02/25/1998
	AC4	5,348,886	09/20/1994	Lee et al.	435	320.1	09/04/1992
	AD4	6,171,861	01/09/2001	Hartley et al.	435	455	01/12/1998
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FOREIGN PATENT DOCUMENTS							
EXAMINER INITIAL		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUB-CLASS	TRANSLATION
	AL4	WO 99/10488	03/04/1999	WIPO			Yes No
	AM4	WO 00/12687	03/09/2000	WIPO			Yes No
	AN4	EP 1 035 208	09/13/2000	Europe			Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	4	Argos, P., et al., "The integrase family of site-specific recombinases: regional similarities and global diversity," <i>EMBO J.</i> 5(2):433-440, IRL Press Limited, Oxford, England (1986).
	AS	4	Astumian, et al., "Site-specific recombination between cloned attP and attB sites from the Haemophilus influenza bacteriophage HP1 propagated in recombination deficient <i>Escherichia coli</i> ," <i>J. Bacteriol.</i> 171:1747-1750, American Society for Microbiology, Washington, D.C. (1989).
	AT	4	Atlung, T., et al., "A versatile method for integration of genes and gene fusions into the $\lambda$ attachment site of <i>Escherichia coli</i> ," <i>Gene</i> 107:11-17, Elsevier/North-Holland, Netherlands (1991).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>5</u>	Ausubel, F.M., et al., "Maps of Plasmids pBR322 and pUC19," in <i>Current Protocols in Molecular Biology</i> , John Wiley & Sons, Inc., Boston, MA, (1995).
	AS	<u>5</u>	Ausubel, F.M., et al., "Mutagenesis by the Polymerase Chain reaction," in: <i>Current Protocols in Molecular Biology</i> , John Wiley & Sons, Inc., Boston, MA, pp. 8.5.1-8.5.9 (1995).
	AT	<u>5</u>	Babineau, D. et al., "The FLP Protein of the 2-micron Plasmid of Yeast," <i>J. Biol. Chem.</i> 260:12313-12391, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1985).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>6</u>	Balakrishnan, R., et al., "A gene cassette for adapting <i>Escherichia coli</i> strains as hosts for att-Int-mediated rearrangement and p <sub>L</sub> expression vectors," <i>Gene</i> 138:101-104, Elsevier/North-Holland, Netherlands (January 1994).
	AS	<u>6</u>	Bayley, C.C., et al., "Exchange of gene activity in transgenic plants catalyzed by the Cre-lox site specific recombination system," <i>Plant Mol. Biol.</i> 18:353-361, Dordrecht Kluwer Academic, Boston, MA (1992).
	AT	<u>6</u>	Bethke, B., and Sauer, B., "Segmental genomic replacement by Cre-mediated recombination: genotoxic stress activation of the p53 promoter in single-copy transformants," <i>Nucl. Acids Res.</i> 25:2828-2834, Oxford University Press, Oxford, England (1997).

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	AL						Yes No
	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	7	Bernard, P., and Couturier, M., "Cell Killing by the F plasmid CcdB Protein Involves Poisoning of DNA-topoisomerase II Complexes," <i>J. Mol. Biol.</i> 226:735-745, Academic Press, Inc., New York, NY (1992).
	AS	7	Bernard, P., et al., "Positive Selection of vectors using the F plasmid ccdB killer gene," <i>Gene</i> 148:71-74, Elsevier Science Publishers B.V., Amsterdam, Netherlands (1994).
	AT	7	Betz, U.A.K., et al., "Bypass of lethality with mosaic mice generated by Cre-loxP-mediated recombination," <i>Curr. Biol.</i> 6:1307-1316, Current Biology Ltd., London, England (October 1996).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	8	Bhandari, P. and Gowrishankar, J., "An <i>Escherichia coli</i> host strain useful for efficient overproduction of cloned gene products with NaCl as the inducer," <i>J. Bacteriol.</i> 179:4403-4406, American Society for Microbiology, Washington, D.C. (July 1997).
	AS	8	Black, L.W., "In vitro packaging into phage T4 particles and specific recircularization of phage lambda DNAs," <i>Gene</i> 46:97-101, Elsevier/North-Holland, Netherlands (1986).
	AT	8	Bloch, C.A., et al., "Purification of <i>Escherichia coli</i> Chromosomal Segments without Cloning," <i>Biochem. Biophys. Res. Comm.</i> 223:104-111, Academic Press, Inc., New York, NY (1996).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>2</u>	Bochner, B. R., et al., "Positive Selection for Loss of Tetracycline Resistance," <i>J. Bacteriol.</i> 143:926-933, American Society for Microbiology, Washington, D.C. (1980).
	AS	<u>2</u>	Boyd, A. C., "Turbo cloning: a fast, efficient method for cloning PCR products and other blunt-ended DNA fragments into plasmids," <i>Nucl. Acids Res.</i> 21(4):817-821, Oxford University Press, Oxford, England (1993).
	AT	<u>2</u>	Broach, J. R., et al., "Recombination within the Yeast Plasmid 2 $\mu$ Circle is Site-Specific," <i>Cell</i> 29:227-234, Cell Press, Cambridge, MA (1982).

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	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>10</u>	Brunelli, J. P. and Pall, M. L., "A Series of Yeast/ <i>Escherichia coli</i> $\lambda$ Expression Vectors Designed for Directional Cloning of cDNAs and <i>cre/lox</i> -Mediated Plasmid Excision," <i>Yeast</i> 9:1309-1318, John Wiley, Chichester, NY (1993).
	AS	<u>10</u>	Brunelli, J.P., and Pall, M.L., "Lambda/Plasmid Vector Construction by <i>In Vivo cre/lox</i> -Mediated Recombination," <i>BioTechniques</i> 16(6):1061-1064, Eaton Publishing Company, Natick, MA (June 1994).
	AT	<u>10</u>	Bubeck, P., et al., "Rapid cloning by homologous recombination in vivo," <i>Nucl. Acids Res.</i> 21:3601-3602, Oxford University Press, Oxford, England (1993).

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	AR	<u>11</u>	Buchholz, F., et al., "A simple assay to determine the functionality of Cre or FLP recombination targets in genomic manipulation constructs," <i>Nucl. Acids Res.</i> 24(15):3118-3119, Oxford University Press, Oxford, England (1996).
	AS	<u>11</u>	Buchholz, F., et al., "Different thermostabilities of FLP and Cre recombinases: implications for applied site-specific recombination," <i>Nucl. Acids Res.</i> 24(21):4256-4262, Oxford University Press, Oxford, England (1996).
	AT	<u>11</u>	Bushman, W., et al., "Control of Directionality in Lambda Site Specific Recombination," <i>Science</i> 230:906-911, Association for the Advancement of Science, Washington D.C. (1985).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>12</u>	Campbell, A. M., "Chromosomal Insertion Sites for Phages and Plasmids," <i>J. Bacteriol.</i> 174(23):7495-7499, American Society for Microbiology, Washington, D.C. (1992).
	AS	<u>12</u>	Chapin, S.J., et al., "Differential expression of alternatively spliced forms of MAP4: a repertoire of structurally different microtubule-binding domains," <i>Biochem.</i> 34:2289-2301, American Chemical Society, Washington D.C. (1995).
	AT	<u>12</u>	Chatterjee, P.K., and Coren, J.S., "Isolating large nested deletions in bacterial and P1 artificial chromosomes by <i>in vivo</i> P1 packaging of products of Cre-catalyzed recombination between the endogenous and a transposed loxP site," <i>Nucl. Acids Res.</i> 25:2205-2212, Oxford University Press, Oxford, England (1997).

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	AR	<u>13</u>	Cox, M.M., "The FLP protein of the yeast 2- $\mu$ m plasmid: Expression of a eukaryotic genetic recombination system in <i>Escherichia coli</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 80:4223-4227, National Academy of Sciences of the USA, Washington, D.C. (1983).
	AS	<u>13</u>	Craig, N.L. and Nash, H.A., "The Mechanism of Phage $\lambda$ Site-Specific Recombination: Site-Specific Breakage of DNA by Int Topoisomerase," <i>Cell</i> 35:795-803, Cell Press, Cambridge, MA (1983).
	AT	<u>13</u>	Dale, E.C. and Ow, D.W., "Intra- and intermolecular site-specific recombination in plant cells mediated by bacteriophage P1 recombinase," <i>Gene</i> 91:79-85, Elsevier/North-Holland, Netherlands (1990).

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	AR	<u>14</u>	Dale, E.C. and Ow, D.W., "Gene transfer with subsequent removal of the selection gene from the host genome," <i>Proc. Natl. Acad. Sci. USA</i> 88:10558-10562, National Academy of Sciences of the USA, Washington, D.C. (1991).
	AS	<u>14</u>	Dang, D.T. and Perrimon, N., "Use of a Yeast Site-Specific Recombinase to Generate Embryonic Mosaics in <i>Drosophila</i> ," <i>Develop. Genetics</i> 13:367-375, Wiley-Liss, Inc., New York, NY (1992).
	AT	<u>14</u>	Degryse, E., "In vivo intermolecular recombination in <i>Escherichia coli</i> : application to plasmid constructions," <i>Gene</i> 170:45-50, Elsevier/North-Holland, Netherlands (1996).

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	AR	<u>15</u>	Devine, S. E., and Boeke, J.D., "Efficient integration of artificial transposons into plasmid targets <i>in vitro</i> : a useful tool for DNA mapping, sequencing and genetic analysis," <i>Nucl. Acids Res.</i> 22(18):3765-3772, Oxford University Press, Oxford, England (September 1994).
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	AT	<u>15</u>	Dymecki, S. M., "A modular set of <i>Flp</i> , <i>FRT</i> and <i>lacZ</i> fusion vectors for manipulating genes by site-specific recombination," <i>Gene</i> 171:197-201, Elsevier/North-Holland, Netherlands (June 1996).

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	AR	<u>16</u>	Elledge, S. J., et al., "AYES: A multifunctional cDNA expression vector for the isolation of genes by complementation of yeast and <i>Escherichia coli</i> mutations," <i>Proc. Natl. Acad. Sci. USA</i> 88:1731-1735, National Academy of Sciences of the USA, Washington, D.C. (1991).
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	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>17</u>	Fiering, S., et al., "An "in-out" strategy using gene targeting and FLP recombinase for the functional dissection of complex DNA regulatory elements: Analysis of the $\beta$ -globin locus control region," <i>Proc. Natl. Acad. Sci. USA</i> 90:8469-8473, National Academy of Sciences of the USA, Washington, D.C. (1993).
	AS	<u>17</u>	Filutowicz, M., et al., "Purification of the <i>Escherichia coli</i> integration host factor (IHF) in one chromatographic step," <i>Gene</i> 147:149-150, Elsevier/North-Holland, Netherlands (September 1994).
	AT	<u>17</u>	Francia, M.V., and Lobo, J.M.G., "Gene Integration in the <i>Escherichia coli</i> Chromosome Mediated by Tn21 Integrase (Int21)," <i>J. Bacteriol.</i> 178:894-898, American Society for Microbiology, Washington, D.C. (February 1996).

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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>18</u>	Fukushige, S. and Sauer, B., "Genomic targeting with a positive-selection lox integration vector allows highly reproducible gene expression in mammalian cells," <i>Proc. Natl. Acad. Sci. USA</i> 89:7905-7909, National Academy of Sciences of the USA, Washington, D.C. (1992).
	AS	<u>18</u>	Geoffroy, F., et al., "A new phage display system to construct multicombinatorial libraries of very large antibody repertoires," <i>Gene</i> 151:109-113, Elsevier/North-Holland, Netherlands (December 1994).
	AT	<u>18</u>	Glasgow, A.C., et al., "DNA-binding Properties of the Hin Recombinase," <i>J. Biol. Chem.</i> 264:10072-10082, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1989).

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	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>19</u>	Golic, K. G. and Lindquist, S., "The FLP Recombinase of Yeast Catalyzes Site-Specific Recombination in the Drosophila Genome," Cell 59:499-509, Cell Press, Cambridge, MA (1989).
	AS	<u>19</u>	Gu, H., et al., "Deletion of a DNA Polymerase $\beta$ Gene Segment in T Cells Using Cell Type-Specific Gene Targeting," Science 265:103-106, Association for the Advancement of Science, Washington D.C. (1994).
	AT	<u>19</u>	Guo, F., et al., "Asymmetric DNA bending in the Cre-loxP site-specific recombination synapse," Proc. Natl. Acad. Sci. USA 96:7143-7148, National Academy of Sciences of the USA, Washington, D.C. (1999).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>20</u>	Hardy, S., et al., "Construction of Adenovirus Vectors through Cre-lox Recombination," <i>J. Virol.</i> 71(3):1842-1849, American Society for Microbiology, Washington, D.C. (1997).
	AS	<u>20</u>	Hasan, N., and Szybalski, W., "Control of cloned gene expression by promoter inversion in vivo: construction of improved vectors with a multiple cloning site and the p <sub>tac</sub> promoter," <i>Gene</i> 56:145-151, Elsevier/North-Holland, Netherlands (1987).
	AT	<u>20</u>	Hasan, N., et al., "Escherichia coli genome targeting, I. Cre-lox-mediated in vitro generation of ori <sup>+</sup> plasmids and their in vivo chromosomal integration and retrieval," <i>Gene</i> 150:51-56, Elsevier/North-Holland, Netherlands (December 1994).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>21</u>	Hashimoto-Gotoh, T., et al., "Improved vector, pHSG664, for direct streptomycin-resistance selection: cDNA cloning with G:C-tailing procedure and subcloning of double-digested DNA fragments," <i>Gene</i> 41:125-128, Elsevier/North-Holland, Netherlands (1986).
	AS	<u>21</u>	Hoekstra, M. F., et al., "Shuttle Mutagenesis: Bacterial Transposons for Genetic Manipulations in Yeast," <i>Meth. Enzymol.</i> 194:329-342, Academic Press Inc., New York, NY (1991).
	AT	<u>21</u>	Hoess, R.H., et al., "P1 site-specific recombination: Nucleotide sequence of the recombining sites," <i>Proc. Natl. Acad. Sci. USA</i> 79:3398-3402, National Academy of Sciences of the USA, Washington, D.C. (1982).

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	AT	<u>22</u>	Hoess, R. H., et al., "The role of the loxP spacer region in P1 site-specific recombination," <i>Nucl. Acids Res.</i> 14(5):2287-2300, Oxford University Press, Oxford, England (1986).

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	AT	<u>23</u>	Holt, C.L., and May, G.S., "A novel phage $\lambda$ replacement Cre-lox vector that has automatic subcloning capabilities," <i>Gene</i> 133:95-97, Elsevier/North-Holland, Netherlands (1993).

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	AP						Yes No

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	AR	<u>24</u>	Jaffé, A., et al., "Effects of the ccd Function of the F Plasmid on Bacterial Growth," <i>J. Bacteriol.</i> 163:841-849, American Society for Microbiology, Washington, D.C. (1985).
	AS	<u>24</u>	Kanaar, R., et al., "Gin-Mediated Recombination of Catenated and Knotted DNA Substrates: Implications for the Mechanism of Interaction Between Cis-Acting Sites," <i>Cell</i> 58:147-159, Cell Press, Cambridge, MA (1989).
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	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>25</u>	Kilby, N.J., et al., "Site-specific recombinases: tools for genome engineering," <i>Trends Genet.</i> 9:413-421, Elsevier Science Publishers Ltd., Cambridge, England (1993).
	AS	<u>25</u>	Kim, S., et al., "Lambda Int Protein Bridges Between Higher Complexes at Two Distant Chromosomal Loci attL and attR," <i>Science</i> 256:198-263, Association for the Advancement of Science, Washington D.C. (1992).
	AT	<u>25</u>	Kozak, M., "Comparison of Initiation of Protein Synthesis in Prokaryotes, Eucaryotes, and Organelles," <i>Microbiol. Rev.</i> 47:1-45, American Society For Microbiology, Washington, D.C. (1983).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>26</u>	Kozak, M., "An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs," <i>Nucl. Acids res.</i> 15:8125-8132, Oxford University Press, Oxford, England (1987).
	AS	<u>26</u>	Kozak, M., "Structural features in eukaryotic mRNAs that modulate the initiation of translation," <i>J. Biol. Chem</i> 266:19867-19870, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1991).
	AT	<u>26</u>	Kühn, R., et al., "Inducible Gene Targeting in Mice," <i>Science</i> 269:1427-1429, Association for the Advancement of Science, Washington D.C. (September 1995).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>27</u>	Lafontaine, D., and Tollervey, D., "One-step PCR mediated strategy for the construction of conditionally expressed and epitope tagged yeast proteins," <i>Nucl. Acids Res.</i> 24:2469-2472, Oxford University Press, Oxford, England (1996).
	AS	<u>27</u>	Lakso, M., et al., "Targeted oncogene activation by site-specific recombination in transgenic mice," <i>Proc. Natl. Acad. Sci. USA</i> 89:6232-6236, National Academy of Sciences of the USA, Washington, D.C. (1992).
	AT	<u>27</u>	Lander, E.S., "The New Genomics: Global Views of Biology," <i>Science</i> 274:536-539, Association for the Advancement of Science, Washington D.C. (October 1996).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>28</u>	Landy, A., "Dynamic, Structural, and Regulatory Aspects of $\lambda$ Site-Specific Recombination," <i>Annu. Rev. Biochem.</i> 58:913-949, American Chemical Society, Washington D.C. (1989).
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## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>29</u>	Lee, E.C., et al., "Genetic Analysis of <i>Escherichia coli</i> Integration Host Factor Interactions with Its Bacteriophage $\lambda$ H' Recognition Site," <i>J. Bacteriol.</i> 173:609-617, American Society for Microbiology, Washington, D.C. (1991).
	AS	<u>29</u>	Leong, J.M., et al., "Generation of single base-pair deletions, insertions, and substitutions by a site-specific recombination system," <i>Proc. Natl. Acad. Sci. USA</i> 82:6990-6994, National Academy of Sciences of the USA, Washington, D.C. (1985).
	AT	<u>29</u>	Liu, Q., et al., "The univector plasmid-fusion system, a method for rapid construction o recombinant DNA without restriction enzymes," <i>Curr. Biol.</i> 8:1300-1309, Current Biology Ltd., London, England (1998).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>30</u>	Lorbach, E. et al., "Site-specific Recombination in Human Cells Catalyzed by Phage $\lambda$ Integrase Mutants," <i>J. Mol. Biol.</i> 296:1175-1181, Academic Press, Inc., New York, NY (March 2000).
	AS	<u>30</u>	Luckow, V. A., et al., "Efficient Generation of Infectious Recombinant Baculoviruses by Site-Specific Transposon-Mediated Insertion of Foreign Genes into a Baculovirus Genome Propagated in <i>Escherichia coli</i> ," <i>J. Virol.</i> 67(8):4566-4579, American Society for Microbiology, Washington, D.C. (1993).
	AT	<u>30</u>	Maeser, S., and Kahmann, R., "The Gin recombinase of phage Mu can catalyze site-specific recombination in plant protoplasts," <i>Mol. Gen. Genet.</i> 230:170-176, Springer-Verlag, New York, NY (1991).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>31</u>	Matsuzaki, H., et al., "Chromosome Engineering in <i>Saccharomyces cerevisiae</i> by Using a Site-Specific Recombination System of a Yeast Plasmid," <i>J. Bacteriol.</i> 172:610-618, American Society for Microbiology, Washington, D.C. (1990).
	AS	<u>31</u>	Mahillon, J., et al., "IS231 and other <i>Bacillus thuringiensis</i> transposable elements: a review," <i>Genetica</i> 93:13-26, Dordrecht Kluwer Academic Publishers (November 1994).
	AT	<u>31</u>	McCarthy, J.E. and Brimacombe, R., "Prokaryotic translation: the interactive pathway leading to initiation," <i>Trends Genet.</i> 10:402-407, Elsevier Science Publishers Ltd., Cambridge, England (November 1994).

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	AO						Yes No
	AP						Yes No

## OTHER (Including Author, Title, Date, Pertinent Pages, etc.)

	AR	<u>32</u>	Medberry, S.L., et al., "Intra-chromosomal rearrangements generated by Cre-lox site-specific recombination," <i>Nucl. Acids Res.</i> 23:485-490, Oxford University Press, Oxford, England (1995).
	AS	<u>32</u>	Miki, T. et al., "Control of Segregation of Chromosomal DNA by Sex Factor F in <i>Escherichia coli</i> . Mutants of DNA Gyrase Subunit A Suppress letD ( <i>ccdB</i> ) Product Growth Inhibition," <i>J. Mol. Biol.</i> 225:39-52, Academic Press, Inc., New York, NY (1992).
	AT	<u>32</u>	Mizuuchi, K., and Mizuuchi, K., "Integrative Recombination of Bacteriophage $\lambda$ : In Vitro Study of the Intermolecular Reaction," <i>Cold Spring Harb. Symp. Quant. Biol.</i> 43:1111-1114, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY (1979).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>33</u>	Mizuuchi, M. and Mizuuchi, K., "The extent of DNA sequence required for a functional bacterial attachment site of phage lambda," <i>Nucl. Acids Res.</i> 13:1193-1208, Oxford University Press, Oxford, England (1985).
	AS	<u>33</u>	Mozo, T. and Hooykaas, P. J. J., "Design of a novel system for the construction of vectors for Agrobacterium-mediated plant transformation," <i>Mol. Gen. Genet</i> 236:1-7, Springer-Verlag, New York, NY (1992).
	AT	<u>33</u>	Mullins, L.J., et al., "Efficient Cre-lox linearisation of BACs: applications to physical mapping and generation of transgenic animals," <i>Nucl. Acids Res.</i> 25(12):2539-2540, Oxford University Press, Oxford, England (1997).

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	AR	<u>34</u>	Nagaraja, R. and Weisberg, R. A., "Specificity Determinants in the Attachment Sites of Bacteriophages HK022 and $\lambda$ ," <i>J. Bacteriol.</i> 172:6540-6550, American Society for Microbiology, Washington, D.C. (1990).
	AS	<u>34</u>	Nash, H.A., "Integrative Recombination of Bacteriophage Lambda DNA <i>In Vitro</i> ," <i>Proc. Natl. Acad. Sci. USA</i> 72:1072-1076, National Academy of Sciences of the USA, Washington, D.C. (1975).
	AT	<u>34</u>	Nash, H.A., and Robertson, C.A., "Purification and properties of the <i>Escherichia coli</i> protein factor required for lambda integrative recombination," <i>J. Biol. Chem.</i> 256:9246-9253, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1981).

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	AR	<u>35</u>	Nash, H. A., "Purification and Properties of the Bacteriophage Lambda Int Protein," <i>Meth. Enzymol.</i> 100:210-216, Academic Press Inc., New York, NY (1983).
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	AT	<u>35</u>	Nash, H. and C.A. Robertson, "Heteroduplex substrates for bacteriophage lambda site-specific recombination: cleavage and strand transfer products," <i>EMBO J.</i> 8:3523-3533, IRL Press Limited, Oxford, England (1989).

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	AS	<u>36</u>	Numrych, T. E., et al., "A comparison of the effects of single-base and triple-base changes in the integrase arm-type binding sites on the site-specific recombination of bacteriophage lambda," <i>Nucl. Acids Res.</i> 18:3953-3959, Oxford University Press, Oxford, England (1990).
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	AT	<u>37</u>	Oberto, J., et al., "A segment of the phage HK022 chromosome is a mosaic of other lambdoid chromosomes," Nucl. Acids Res. 22(3):354-356, Oxford University Press, Oxford, England (February 1994).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>38</u>	Oliner, J.D., <i>et al.</i> , "In vivo cloning of PCR products in <i>E. coli</i> ," <i>Nucl. Acids Res.</i> 21:5192-5197, Oxford University Press, Oxford, England (1993).
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	AT	<u>38</u>	Osborne, B.I., <i>et al.</i> , "A system for insertional mutagenesis and chromosomal rearrangement using the Ds transposon and Cre-lox," <i>Plant J.</i> 7:687-701, Oxford Bios Scientific Publishers And Blackwell Scientific Publications In Association With The Society For Experimental Biology, Oxford, England (1995).

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FORM PTO-1449

## INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO.  
0942.4680003APPLICATION NO.  
09/517,466APPLICANT  
Hartley et al.FILING DATE  
March 2, 2000GROUP  
1655

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EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUB- CLASS	FILING DATE
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

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	AR	<u>39</u>	Padgett, K. A. and Sorge, J. A., "Creating seamless junctions independent of restriction sites in PCR cloning," <i>Gene</i> 168:31-35, Elsevier/North-Holland, Netherlands (February 1996).
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>41</u>	Pichel, J. G., et al., "Timing of SV40 oncogene activation by site-specific recombination determines subsequent tumor progression during murine lens development," <i>Gene</i> 8:3333-3342, Elsevier/North-Holland, Netherlands (1993).
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	AR	<u>43</u>	Reed, R.R., "Transposon-Mediated Site-Specific Recombination: A Defined in Vitro System," Cell 25:713-719, Cell Press, Cambridge, MA (1981).
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	AR	<u>45</u>	Sauer, B., et al., "Site-specific insertion of DNA into a pseudorabies virus vector," <i>Proc. Natl. Acad. Sci. USA</i> 84:9108-9112, National Academy of Sciences of the USA, Washington, D.C. (1987).
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
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	AM						Yes No
	AN						Yes No
	AO						Yes No
	AP						Yes No

OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>53</u>	Thompson, J. F., et al., "Mutations in an Integration Host Factor-Binding Site: Effect on Lambda Site-Specific Recombination and Regulatory Implications," <i>J. Bacteriol.</i> 168:1343-1351, American Society for Microbiology, Washington, D.C. (1986).
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
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	AT	<u>60</u>	Jeong, J.-H., et al., "Cloning and nucleotide sequencing of the genes, <i>rplU</i> and <i>rpmA</i> , for ribosomal proteins L21 and L27 of <i>Escherichia coli</i> ," <i>J. DNA sequencing and Mapping</i> 4:59-67, Harwood Academic Publishers GmbH, Switzerland (1993).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
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	AT	<u>61</u>	Mackie, G.A., "Nucleotide Sequence of the Gene for Ribosomal Protein S20 and Its Flanking Regions," <i>J. Biol. Chem.</i> 256:8177-8182, American Society for Biochemistry and Molecular Biology, Inc., Baltimore, MD (1981).

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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
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OTHER (Including Author, Title, Date, Pertinent Pages, etc.)			
	AR	<u>63</u>	Jayaram, M., "The Int family of site-specific recombinases: Some thoughts on a general reaction mechanism," <i>J. Genet.</i> 67:29-36, Indian Academy Of Sciences Bangalore, Bangalore, India (1988).
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	AO						Yes No
	AP						Yes No

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	AR	<u>64</u>	Pending U.S. Non-Provisional Patent Application No. 09/233,492, filed January 20, 1999.
	AS	<u>64</u>	Pending U.S. Non-Provisional Patent Application No. 09/296,280, filed April 22, 1999.
	AT	<u>64</u>	Pending U.S. Non-Provisional Patent Application No. 09/296,281, filed April 22, 1999.

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	AP						Yes No

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	AR	<u>65</u>	Pending U.S. Non-Provisional Patent Application No. 09/432,085, filed November 02, 1999.
	AS	<u>65</u>	Pending U.S. Non-Provisional Patent Application No. 09/438,358, filed November 12, 1999.
	AT	<u>65</u>	Pending U.S. Non-Provisional Patent Application No. 09/498,074, filed February 4, 2000.

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	AR	<u>66</u>	Pending U.S. Non-Provisional Patent Application No. 09/518,188, filed March 2, 2000.
	AS	<u>66</u>	Pending U.S. Non-Provisional Patent Application No. 09/648,790, filed August 28, 2000.
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	AR	<u>67</u>	Pending U.S. Non-Provisional Patent Application No. 09/732,914, filed December 11, 2000.
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EXAMINER	DATE CONSIDERED
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**EXAMINER:** Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.